

## EBOLA

# The great ape gamble

*Ebola could pose a grave health threat to gorillas in Africa. Vaccination seems like a smart solution, but dosing the animals in the wild poses major challenges.*

BY CASSANDRA WILLYARD

In 2003, Damien Caillaud arrived in the Congo and made his way deep into Odzala-Kokoua National Park, a pristine stretch of tropical forest that covers more than 13,000 square kilometres. The park boasted one of the highest densities of gorillas in the world, and Caillaud, then a 24-year-old PhD student, was there to observe them in one particular forest clearing. “Every day, I could observe at least one gorilla group,” says Caillaud, who is now at the University of California, Davis.

In January 2004, however, Caillaud noticed a change. The apes began to disappear. “I started having a few days once in a while where I wouldn’t see gorillas — and then that turned into sometimes a week,” he says. By May, Caillaud was worried. He knew that there had been an Ebola outbreak in a nearby village, and he suspected that the disease might also be to blame for the disappearance of the gorillas. Caillaud didn’t find many carcasses in the forest, but he could see the impact nonetheless. Of the 364 gorillas that had been regulars at his study site, fewer than 30 remained.

The phenomenon wasn’t unique to Odzala-Kokoua. In the nearby Lossi Sanctuary close to the Gabon border, a research team reported that more than 200 gorillas disappeared between 2002 and 2004. Several carcasses tested positive for Ebola<sup>1</sup>.

To Peter Walsh, a quantitative ecologist at the University of Cambridge, UK, the tragedy was a call to arms. Walsh launched a campaign to convince primatologists, conservationists and the public that the survival of Africa’s great apes depends on vaccination against diseases such as Ebola. Now, more than a decade after that outbreak, Walsh and his team have a vaccine that is ready to be field-tested. He sees the trial as an important first step to introducing a host of medical interventions. “If we don’t start dealing with the disease threats, then the conservation outlook for these species is very dim,” he says. But Walsh is finding it hard to make headway: many experts say that mass vaccination isn’t feasible, and his attempts to roll out the vaccine have come up against a number of obstacles.

## VACCINE HUNTING

Walsh’s interest in Ebola, an often fatal viral disease that affects both humans and apes, began in 2001. He had been hired to help officials in Gabon establish a national-park system.



Veterinary surgeons from the Gorilla Doctors team clean a wound after removing a snare.

Soon after he arrived, Ebola struck the north-eastern part of the country. The virus killed dozens of people, and Walsh began to hear reports of apes that had died of Ebola too. To assess the impact of the disease, Walsh and his colleagues compared wildlife survey data collected in the early 1980s with those from 2000 (ref. 2). The analysis suggested that the population of apes at the survey sites had halved over the two decades — and that one of the best predictors of ape density was distance from the site of a human Ebola outbreak. “The stark truth is that if we do not act decisively our children may live in a world without wild apes,” Walsh and his colleagues wrote.

In 2006, Walsh’s group reported that the Ebola epidemic that had struck Odzala-Kokoua and Lossi had claimed the lives of as many as 5,000 western lowland gorillas<sup>1</sup> (*Gorilla gorilla gorilla*) over an area that spanned nearly 5,000 km<sup>2</sup>. In 2008, the International Union for Conservation of Nature listed the species as critically endangered.

To Walsh, the response seemed obvious:

scientists would have to find a way to vaccinate the apes. So in 2011, he embarked on a novel experiment<sup>3</sup>. His team injected six chimpanzees with an experimental Ebola vaccine that had been developed for humans — thought to be the first time captive chimps had been vaccinated with the goal of preventing the spread of disease among apes. The researchers didn’t challenge the protection directly by exposing the chimps to Ebola — that experiment wouldn’t have been ethical or feasible — but the vaccine had already been shown to protect macaque monkeys from the virus. Walsh showed that the apes developed antibodies against Ebola, and that transferring these antibodies to mice infected with the virus improved the rodents’ survival.

Walsh knew that an injectable vaccine would be hard to administer in the wild. So in 2015, he partnered with virologist Matthias Schnell at Thomas Jefferson University in Philadelphia, Pennsylvania, who had previously tweaked an oral rabies vaccine to carry an Ebola protein. The team vaccinated ten chimps at the University of Louisiana’s New Iberia Research Center:

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four received an injectable version of the vaccine, and six were given the oral version<sup>4</sup>. All the chimps developed immune responses similar to those observed in Walsh's 2011 study, and had no serious adverse effects.

The trial lasted 28 days. Walsh would have liked to have conducted a longer study, but he had to cut the experiment short because the United States added captive chimps to the endangered-species list — a move that barred most biomedical research. Soon after, the National Institutes of Health retired all of its remaining research chimpanzees. The decision put Walsh in a bind. He had hoped to develop a heat-stable version of the vaccine, and to do the experiment one more time to convince people in the conservation community of the vaccine's safety and efficacy. Research aimed at benefiting wild chimpanzees isn't prohibited under the new rule, but Walsh doesn't think he will be able to convince any of the facilities that still have chimps — universities, zoos and sanctuaries — to apply for the permit now needed to go forward with another trial. "One side won't let us use captive animals for tests," he says. "The other side won't let us protect the wild animals without captive-animal tests."

### MISSION IMPOSSIBLE

As researchers and veterinary surgeons who have worked in Africa point out, developing an effective vaccine is just the first step. Walsh must now figure out how to deliver it. "The vaccination programme is always more difficult than making a vaccine," says William Karesh, a vet and executive vice-president at the non-profit environmental health organization EcoHealth Alliance in New York City.

The oral rabies vaccine, the starting point for Schnell's Ebola vaccine, is often packaged in bait and dropped by plane. Germany eliminated fox rabies in this manner in a campaign between 1983 and 2008. But Africa is "a really different scenario", says Thomas Gillespie, a global-health researcher at Emory University in Atlanta, Georgia. Many of Africa's apes inhabit vast areas of roadless forest. "You have landscapes that are potentially tens or hundreds of times larger than they are elsewhere in the world and which are incredibly remote," says Rich Bergl, who oversees the conservation and research programme at North Carolina Zoo in Asheboro and studies gorilla conservation in Africa. Walsh admits that air-dropping the vaccine would not be cost-effective. But he thinks that it could be distributed by field teams or drones.

Even if researchers could find a way to get the vaccine to the apes, there's no guarantee that the animals would consume it. Gorillas and chimpanzees are picky eaters. Gillespie has seen wild chimps pluck what seem to be perfectly ripe figs off a tree and then toss them away. "They'll pull it, they'll smell it, and they'll drop it — and they'll do this repeatedly," he says.

Walsh thinks that these hurdles can be

overcome, given some time and money. He has developed a sweet bait that he says is promising — especially if suspended in the air to avoid consumption by rats. He thinks that there might be high-tech workarounds too. For example, if he had a video feed of a spot where gorillas tend to congregate, he could use a remote trigger to release oral bait or spray the gorillas with a sugary solution loaded with the vaccine.

Meanwhile, Michael Jarvis, a virologist at Plymouth University, UK, is working on an Ebola vaccine that could eliminate many of the delivery concerns. The 'self-disseminating' vaccine relies on a herpes virus that could spread from ape to ape — no bait or needles required. "If it works, it will change how we can vaccinate animals, and how we can actually control emerging diseases," Jarvis says.

Even if vaccination were feasible, however, it's not clear what impact it would have on ape populations. Deploying a new vaccine on a large



Peter Walsh and an infant gorilla at a gorilla reintroduction site in the Congo.

scale could have unforeseen consequences, Bergl says.

And although Ebola has been a hot topic recently because of the 2014–16 outbreak that killed more than 10,000 people in West Africa, Gillespie points out that there hasn't been a confirmed case of Ebola in wild apes in more than a decade. "There's potential for it to have an impact on a grand scale," he says, but other dangers are more imminent, he contends. "Apes are far more likely impacted by the bushmeat trade or respiratory illness," he says.

Walsh, however, defends his quest. "Do we need to develop the capacity to vaccinate against infectious diseases in great apes? The answer is definitively yes," he says. Ebola is just a place to start.

### BABY STEPS

Despite the difficulties, conservationists generally favour research on an Ebola vaccine for wild apes<sup>5</sup>. "We've been talking about this for a long time," says Patricia Reed, a vet who managed the

Wildlife Conservation Society's gorilla-health programme in central Africa. And "We're starting for the first time to see vaccines that have characteristics that are really appealing to us."

In the Virunga Mountains in Rwanda, many mountain gorillas (*Gorilla beringei beringei*) are already subject to health interventions. Vets called the Gorilla Doctors administer antibiotics to treat life-threatening bacterial infections and anaesthetize apes to remove snags. In 1988, this group inoculated about 70 gorillas against measles after 25 animals developed respiratory infections, 3 of which died<sup>6</sup>. Although it was not clear whether measles caused the illness, the outbreak subsided, and the trial demonstrated that wild apes could be vaccinated. "There's no doubt that vaccines play a role when there's an outbreak," says Mike Cranfield, the vet who leads the Gorilla Doctors team.

Walsh hopes to build on the Gorilla Doctors' case study. If he can prove that the Ebola vaccine works in wild apes, he thinks that the door will open to even more interventions — vaccines against childhood illnesses such as measles and antiparasite medications, for example.

At each turn, however, Walsh seems to hit another roadblock. He had planned to conduct a small field trial at a tourist camp called Ngaga in Odzala. The gorillas there are used to humans and are constantly monitored, so vaccine-loaded bait would not have to sit out in the sun. But Walsh says that he had to scrap that plan after scientists from the Wildlife Conservation Society in New York City wrote an online article<sup>7</sup> about inoculating apes against Ebola that called wildlife vaccination "risky business". Walsh viewed it as a move to derail his trial. But Kenneth Cameron, one of the authors, says that the article was a response to an apparent "mad dash to get a vaccine out and distribute it". Cameron says he and his colleagues wanted to urge "an abundance of caution before we release something into the environment that could have negative consequences for any other species".

But Walsh says that the vaccine is safe, and he plans to push ahead with or without the support of the conservation community. He sees this effort as extending beyond Ebola, with larger implications for keeping wild apes healthy "I've got to just get on and do it," he says, "and show that it works." ■

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